Remarks

Rejection Under 35 U.S.C. § 102

Claims 1-4, 7, 8, 12, 13, and 15-18 were rejected under 35 U.S.C. § 102(e) as being

anticipated by U.S. Patent No. 6,770,323 to Genzer ("Genzer"). It appears that the Examiner

intended to *only* reject claims 1-4, 7, 8 and 12 under 35 U.S.C. § 102(e) over Genzer. The

Examiner does not provide any discussion as to the basis for the rejection under 35 U.S.C. §

102(e) of claims 13 and 15-18. Further, Examiner acknowledges that "Genzer fails to teach that

the gradient is radially symmetrical." (Office Action at page 6). Therefore Applicants response

focuses on claims 1-4, 7, 8 and 12. Applicants request clarification of this rejection. Further,

Applicants respectfully traverse this rejection to the extent that it is applied to the claims as

amended.

Claim 1

Claim 1 has been amended to include the step of selecting a speed at which the substrate

will be exposed to a solution containing the first adsorbate, wherein the speed is selected based

on the absorption kinetics of the first adsorbate. Support for this amendment can be found in the

specification at least at page 4, lines 12-13. Claim 1 was further amended to insert the phrase

"advancing front" to clarify that the substrate is exposed to the advancing front of the solution

for a sufficient period of time to adsorb the first adsorbate onto the surface. Thus, claim 1 as

amended describes more clearly the steps involved in the claimed method. Applicants believe

that it is proper for the present amendment to be entered since it places the claims in better form

for appeal, does not raise any new issues, and does not require further consideration or search.

Genzer

Genzer discloses methods for forming chemical gradients on substrates. Genzer focuses

on using vapor deposition methods to form a gradient, and contains limited disclosure with

respect to using liquids.

With respect to applying a liquid to the surface, Genzer discloses exposing the surface of

the substrate to a liquid bath (Genzer, col. 4, lines 57-58) and notes that the "fluid may be

introduced to the surface with a fluid concentration gradient so that the first distribution [of the

component on the surface] is a corresponding [...] gradient of the component [in the fluid]."

(Genzer, col. 4, lines 60-63) In this embodiment, the liquid bath contains the component in a

fluid concentration gradient, i.e. a portion of the fluid bath contains a greater concentration of the

component, while another portion of the fluid bath contains a reduced concentration of the

component. This concentration gradient is analogous to the drink referred to as a "Tequila

Sunrise". As noted in the attached description from the internet, this drink is prepared by adding

tequila and orange juice to a glass, and then slowly pouring grenadine into the glass; the

grenadine and orange solids settle, creating variations in colors in the drink that mimic a sunrise.

Similarly, Genzer's liquid bath contains variations in concentration of the component. When the

surface of the substrate is exposed to the liquid bath, the component is deposited on the surface

in a concentration gradient that corresponds with the fluid concentration gradient in the liquid bath.

At col. 14, lines 36-41, Genzer discloses an optional method for forming a surface containing two gradients. This method involves exposing the surface of the substrate to a liquid source and to a vapor source, either at the same time or at different times. Genzer does not further define the method by which the liquid source is used to form a concentration gradient. Thus, it appears that Genzer is using a liquid source having a fluid concentration gradient, as described at col. 4 of the patent and discussed above. Further, Genzer does not describe the length of time that the substrate is exposed to the liquid source. Since Genzer is merely exposing the substrate to a liquid source having a fluid concentration gradient to create a substrate with the same concentration gradient, the entire substrate would likely be in contact with the liquid source for essentially the same time period to allow the component to deposit on the surface of the substrate in a concentration gradient that corresponds with the fluid concentration gradient in the liquid bath.

In contrast to Genzer's method, claim 1 requires (1) selecting a speed at which the substrate will be exposed to an advancing front of a first solution comprising a first adsorbate, wherein the speed is selected based on the absorption kinetics of the first adsorbate, and (2) exposing a substrate to the advancing front of the first solution for a time period sufficient to adsorb the first adsorbate onto the surface of the substrate in an amount decreasing in concentration from a first area on the substrate to a second area on the substrate.

First, Genzer does not disclose selecting the speed for exposing the substrate to the liquid bath. Therefore Genzer does not disclose every element of the claimed method. Further, Genzer only broadly mentions exposing the substrate to a liquid bath, and mentions dipping the substrate into the liquid bath. Genzer does not disclose exposing the substrate to an advancing front of the liquid at the rate specified in claim 1, *i.e.* for a time period sufficient to adsorb the first adsorbate onto the surface of the substrate in an amount decreasing in concentration from a first area on the substrate to a second area on the substrate. Genzer describes a different method than the claimed method for forming one or more gradients on a substrate. Therefore claim 1 and its dependent claims, claims 2-4, 7, 8, and 12, are novel in view of Genzer.

Claims 2, 7, 8 and 12

Further, with respect to claim 2 and its dependent claims, Genzer discloses forming two gradients using two vapor sources or a liquid source in combination with a vapor source (*see* Genzer, col. 14, lines 21-33 and lines 36-41).. Genzer does not disclose using two solutions to form two gradients on a substrate, as required by claim 2 and its dependent claims. Therefore, for at least this additional reason, claim 2 and its dependent claims, claims 7, 8 and 12, are novel over Genzer.

Rejection Under 35 U.S.C. § 103

Claim 10 was rejected under 35 U.S.C. § 103(a) as being obvious over Genzer, in view of U.S. Patent No. 6,242,264 to Natan *et al.* ("Natan"). Claim 11 was rejected under 35 U.S.C. § 103(a) as being obvious over Genzer, in view of U.S. Patent No. 5,656,034 to Kochersperger *et*

al. ("Kochersperger"). Claims 13 and 15-18 were rejected under 35 U.S.C. § 103(a) as being

obvious over Genzer, in view of U.S. Publication No. 2002/0194930 to Crosby et al. ("Crosby").

Applicants respectfully traverse this rejection to the extent that it is applied to the claims as

amended.

Legal Standard

When applying 35 U.S.C. § 103, the following tenets of patent law must be adhered to:

(a) determining the scope and contents of the prior art;

(b) ascertaining the differences between the prior art and the claims in issue;

(c) resolving the level of ordinary skill in the pertinent art; and

(d) evaluating evidence of secondary considerations.

Graham v. John Deere, 383 US 1, 17-18, 148 U.S.P.Q. 459, 467 (1966). These four factors are

traditionally referred to as the Graham factors.

The Graham factors were affirmed by the U.S. Supreme Court in *KSR International Co.*

v. Teleflex, Inc., 127 S. Ct. 1727, 82 U.S.P.Q.2d 1385 (2007). In its analysis of the obviousness

standard, the Court did not totally reject the Federal Circuit's prior use of "teaching, suggestion,

or motivation" as a factor in the obviousness analysis. Rather, the Court recognized that a

showing of "teaching, suggestion, or motivation" to combine the prior art to meet the claimed

subject matter may provide a helpful insight in determining whether the claimed subject matter is

obvious under 35 U.S.C. § 103(a).

The Court also warned against the use of hindsight analysis in making an obviousness determination. The Court stated, "A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning." *KSR*, 127 S. Ct. at 1742, citing *Graham*, 383 U.S. at 36 (warning against a "temptation to read into the prior art the teachings of the invention in issue" and instructing courts to "'guard against slipping into the use of hindsight'" (quoting M*onroe Auto Equipment Co. v. Heckethorn Mfg. & Supply Co.*, 332 F.2d 406, 412, 141 U.S.P.Q. 549 (6th Cir. 1964))).

Claim 10 is nonobvious in view of the combination of Genzer with Natan

Claim 10 depends from claim 1 and specifies that the surface of the substrate is exposed to the first solution using a linear-motion drive.

Genzer

As noted above, Genzer does not disclose the claimed method for preparing a surface-chemical gradient on a substrate. Genzer focuses on vapor deposition methods. In fact, Genzer generally teaches away from using liquids to form chemical gradients, noting that prior techniques "are typically rather cumbersome and involve various 'wet chemistry' surface treatments, which is [*sic*] often times hard to control and not applicable to all materials." (Genzer, col. 1, lines 59-62) Genzer explains that its goal is to "develop methods that would both eliminate the 'wet chemistry' environment and produce surfaces with reproducible and tunable surface properties." (Genzer, col. 1, lines 62-65)

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With respect to using liquids in the method for forming a surface gradient, in one

embodiment, Genzer uses a liquid bath that contains a liquid concentration gradient. The only

disclosure possibly relating to an advancing front is the mention of "dipping in a liquid bath" at

col. 14, line 37. However, as noted above, Genzer does not disclose the rate at which the

substrate is dipped into the bath. Since Genzer is merely exposing the substrate to a liquid

source having a fluid concentration gradient for the purpose of creating a substrate with the same

concentration gradient, the entire substrate would likely be in contact with the liquid source for

essentially the same time period to allow the component to deposit on the surface of the substrate

in a concentration gradient that corresponds with the fluid concentration gradient in the liquid

bath.

In another embodiment, Genzer first forms a homogenous coating on the surface. No

gradient is formed due to the exposure of the substrate to the liquid; rather a gradient is formed

with the substrate is allowed to contract (*see* Genzer, col. 12, lines 58-64 and Figures 4(c) and

4(d)).

Natan

Natan's method is directed at attaching particles on a surface. Natan discloses methods

for forming self-assembled metal colloid monolayers on organics substrates (*see e.g.* Natan, col.

1, lines 14-15; col. 3, lines 30-32). The substrate is modified by first generating hydroxyl or

oxide groups on the surface and then by polymerizing bifunctional organosilanes on the surface.

Then the polymer-derivatized substrate is immersed into a solution of colloidal metal particles

and surface assembly spontaneously occurs (*see* Natan, col. 3, lines 2-16). The self-assembling

monolayers are not adsorbed onto the surface. Further, Natan does not disclose forming surface

chemical gradients.

As noted above, Genzer does not disclose the claimed method. Further, Natan does not

cure the deficiencies of Genzer. Although Natan discloses the use of a motorized translational

stage for immersion (*see* Natan, col. 40, lines 54-55), such a device would not serve any purpose

with Genzer's methods.

In one embodiment, Genzer exposes a substrate to a liquid bath that contains a liquid

concentration gradient to deposit the component on the substrate in a concentration gradient that

corresponds with the liquid concentration gradient in the liquid bath. It appears that the entire

substrate would likely be in contact with the liquid source for essentially the same time period to

allow the component to deposit on the surface of the substrate in a concentration gradient that

corresponds with the fluid concentration gradient in the liquid bath. There is no benefit to

control the dipping procedure using a motorized translational stage for immersion since this

would result in the production of a different concentration gradient on the surface of the

substrate.

In another embodiment, Genzer first forms a homogenous coating on the surface, and

then allows the surface to contract, thereby forming a gradient (*see* Genzer, col. 12, lines 58-64

and Figures 4(c) and 4(d)). There is no benefit to controlling the exposure to the surface to a

liquid source in this method since a homogenous coating is formed.

Further, Natan does not disclose forming chemical gradients and does not adsorb a component onto a substrate. Thus, Genzer and Natan are directed at forming different materials using different methods.

Thus, it would not be obvious to one of ordinary skill in the art to modify Genzer's method to include (1) selecting a speed at which the substrate will be exposed to an advancing front of a first solution comprising a first adsorbate, wherein the speed is selected based on the absorption kinetics of the first adsorbate, and (2) exposing a substrate to the advancing front of the first solution using a linear-motion drive, as required by claim 10.

Therefore claim 10 is nonobvious over Genzer in view of Natan.

Claim 11 is nonobvious in view of the combination of Genzer with Kochersperger

Claim 11 depends from claim 1 and specifies that the surface of the substrate is exposed to the first solution using a syringe pump.

Genzer

Genzer's disclosure is discussed above.

Kochersperger

Kochersperger discloses a syringe pump designed for delivery of small volumes (*e.g.* 1 to 10 µl) at high pressure (Kochersperger, abstract and col. 1, lines 10-13). Kochersperger's syringe pump is designed for micro-scale separations in analytical chemistry (Kochersperger, col. 1, lines 6-13). Kochersperger does not disclose the formation of surface chemical gradients, nor the adsorption of a component onto a substrate.

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As noted above, Genzer does not disclose the claimed method. Further, Kochersperger does not cure the deficiencies of Genzer. Although Kochersperger discloses a particular syringe pump, such a device would not serve any purpose with Genzer's methods.

In one embodiment, Genzer exposes a substrate to a liquid bath that contains a liquid concentration gradient to deposit the component on the substrate in a concentration gradient that corresponds with the liquid concentration gradient in the liquid bath. It appears that the entire substrate would likely be in contact with the liquid source for essentially the same time period to allow the component to deposit on the surface of the substrate in a concentration gradient that corresponds with the fluid concentration gradient in the liquid bath. There is no benefit to control the dipping procedure using a syringe pump since this would result in the production of a different concentration gradient on the surface of the substrate.

In another embodiment, Genzer first forms a homogenous coating on the surface, and then allows the surface to contract, thereby forming a gradient (*see* Genzer, col. 12, lines 58-64 and Figures 4(c) and 4(d)). There is no benefit to controlling the exposure to the surface to a liquid source in this method since a homogenous coating is formed.

Further Kochersperger does not adsorb a component onto a substrate. It appears that the volumes delivered with Kochersperger's device are likely too small to be useful for forming chemical gradients on macroscopic surfaces. Thus, Genzer and Kochersperger are directed at different methods.

Thus, it would not be obvious to one of ordinary skill in the art to modify Genzer's method to include (1) selecting a speed at which the substrate will be exposed to an advancing front of a first solution comprising a first adsorbate, wherein the speed is selected based on the absorption kinetics of the first adsorbate, and (2) exposing a substrate to the advancing front of the first solution using a syringe pump, as required by claim 11.

Therefore claim 11 is nonobvious over Genzer in view of Kochersperger.

Claims 13 and 15-18 are nonobvious in view of the combination of Genzer with Crosby

Independent claims 13, 15 and 16 specify that the surface gradient is radially symmetrical. Independent claim 13 defines a method of using a surface-chemical gradient for biological analysis by exposing the surface-chemical gradient to cells. The surface-chemical gradient is radially symmetrical and contains a first adsorbate in an amount decreasing in concentration from a first area on the substrate to a second area on the substrate and a second adsorbate in an amount increasing in concentration from the first area on the substrate to the second area on the substrate.

Independent claim 15 defines a method of using a surface-chemical gradient for analysis by exposing the surface-chemical gradient to a molecule. The surface-chemical gradient is radially symmetrical and contains a first adsorbate in an amount decreasing in concentration from a first area on the substrate to a second area on the substrate and a second adsorbate in an amount increasing in concentration from the first area on the substrate to the second area on the substrate. And, the molecule preferentially binds to with the first adsorbate.

Independent claim 16 defines a surface-chemical gradient on the surface of a substrate. The surface-chemical gradient is radially symmetrical and contains a first adsorbate in an amount decreasing in concentration from a first area on the substrate to a second area on the substrate and a second adsorbate in an amount increasing in concentration from the first area on the substrate to the second area on the substrate.

Dependent claims 17 and 18 depend from claim 16.

Genzer

Genzer's disclosure is discussed above. The Examiner acknowledges that Genzer does not disclose radially symmetric surface chemical gradients (Office Action, p. 6).

Crosby

Crosby discloses a method of measuring the adhesive strength of polymeric materials that are arranged in a combinatorial library (Crosby, abstract). Crosby creates an array of curved surfaces, referred to as 'lenses', on a surface and contacts the lens array with a substrate containing a polymeric material to be tested thereon. (*see* Crosby, para. 0026 and 0027). The substrate is then separated from the lens array in a controlled manner. During the contact step and the separation step, a variety of data are collected, including each contact point between the tested polymeric material and each individual lens. This information is used to quantitatively determine the adhesion energy of the tested polymeric material. (Crosby, para. 0029)

Arrays of lenses are not equivalent to surface chemical gradients. Arrays are discrete structures that can be inserted in the desired location on a surface. Crosby does not disclose the

formation of surface chemical gradients, nor the adsorption of a component onto a substrate.

Thus the disclosure of different arrangements in the lens array has no relationship to the structure

of a surface chemical gradient.

Crosby discloses the test conditions can be modified in a controlled manner to determine

the optimal adhesion conditions. The use of "different parameter gradients with respect to

physical, material and environmental characteristics along a desired axial, radial and/or

orthogonal direction", such as "temperature, surface energy, strain, rate of strain, molecular

weight of a polymer used, surface topography, surface roughness, chemical functionality, metal

coating composition, ceramic coating composition" (Crosby, para. 0035), bears no relationship

to surface-chemical gradients on a surface.

Contrary to the Examiner's assertion, Crosby does not disclose surface-chemical

gradients, let alone radially symmetrical surface chemical gradients. Further, there is no

indication in Crosby that axial surface chemical gradients are equivalent to radially symmetric

surface chemical gradients.

As noted above, Genzer does not disclose the methods of using a surface chemical

gradient defined by claims 13 and 15. Further, Genzer does not disclose the radially symmetrical

surface chemical gradient defined by claims 16-18. Further, Crosby does not cure the

deficiencies of Genzer. Crosby's comments regarding arrays and modifying test conditions bear

no relationship with methods of using chemical gradients or chemical gradients.

Thus, Genzer and Crosby are directed at forming different materials using different methods. Therefore, it would not be obvious to one of ordinary skill in the art to modify Genzer's methods and materials to form and use a radially symmetric surface chemical gradient.

Therefore claims 13 and 15-18 are nonobvious over Genzer in view of Crosby.

Additional Amendments to the Claims

Claim 13 has been amended to correct a typographical error by deleting an extra comma from the end of the claim.

Entry of the amendment and allowance of claims 1-18, as amended, is respectfully solicited.

Respectfully submitted,

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